REMARKS/ARGUMENTS

Status of the Claims

Claims 107 and 108 are pending. Claims 109 -119 are new. Support is found throughout the specification and in the claims as filed. For example, suppoer for claims 109 and 110 is found in the claims and specification as filed; see for example, paragraphs 98-102 and Table 2. Support for claims 111 and 112 is found at least in paragraph 81. Support for claims 113-118 is found at least in paragraph 102. Support for claim 119 is found at least in paragraph 88. No new matter is introduced by way of this amendment.

Applicants appreciate the Examiner's clarification of the discrepancies in the previous Response to Final Office Action. Indeed, the response was to be directed to the instant application No.: 09/855,320. In addition, Applicants appreciate the withdrawal of rejections under 35 U.S.C. § 112, first paragraph for enablement and written description as well as withdrawal of rejections under 35 U.S.C. § 103.

Specification

The Examiner objected to the disclosure because it contains hyperlinks. In response, Applicants have deleted reference to hyperlinks. Applicants respectfully request the Examiner withdraw the objection.

New Matter/Objection to the Specification

The Examiner suggests that the previous amendment of the specification contains New Matter. The Examiner states that in response to the office action this "New Matter" must be canceled. It appears that the reason the Examiner considers the amendment to include New Matter is because a perusal of the section cited by Applicants in support of the amendment "clearly reveals that the applicants' [sic] have not explicitly stated 'incorporated by reference'". Thus, the Examiner "deems that amendments to the specification and claims as new-matter." See page 4 of the June 9, 2008 Office Action. Applicants respectfully disagree.

In the Response to Office Action of January 18, 2008, Applicants amended the

specification on page 26. In support of this amendment Applicants pointed to page 24, lines 9-10 and page 46, lines 22-23. However, the citation to page 24 was in error. Applicants intended to refer to page 26, lines 9-10. Page 26, lines 9-10 recites:

"...and the βGal(1→4)βGlcNAc α1→3)fucosyltransferases (FucT-IV, FucT-V, FucT-VI and FucT-VII, E.C. No. 2.4.1.65) which are found in human serum." This is the support for the sequences of the fucosyltransferase.

Moreover, the incorporation by reference is found at page 46, lines 22-23. As such, Applicants submit that neither the claims nor specification include New Matter. Accordingly, Applicants have not canceled the subject matter of this amendment. Applicants respectfully request the Examiner to withdraw this New Matter/Objection of the specification and the claims.

New Matter/Claim Rejections 35 U.S.C. § 112

Claims 107 and 108 are rejected under 35 U.S.C. §112, first paragraph, for lack of written description. Specifically, the claims are rejected for the phrase "SEQ ID NO: 1 and SEQ ID NO: 2". Applicants respectfully traverse.

As noted above, Applicants submit that the amendment of the specification and claims in the Response to Final Office Action of January 18, 2008 did not contain New Matter because the sequences in question were incorporated by reference. The proper support for the amendment is set forth above. In view of this correction, Applicants respectfully request the Examiner to withdraw this rejection.

Rejection Under 35 U.S.C. §102

Claim 107 is rejected under 35 U.S.C. § 102(b), as being anticipated by Lowe JB[1] (U.S. Patent 5,324,663 ('663)) or Lowe[2] (U.S. Patent 5,770,420 ('420)). Applicants respectfully traverse.

Claim 107 is directed to a method for modifying the fucosylation pattern of a recombinant glycopeptide comprising an acceptor, the method includes contacting a full-length recombinant glycopeptide with a reaction mixture that comprises a fucose donor moiety and a fucosyltransferase under appropriate conditions *in vitro* to transfer fucose from the fucose donor moiety to the acceptor moiety, such that the glycopeptide has a substantially

uniform fucosylation pattern, wherein the acceptor moiety is Galβ1,4GlcNAc-OR or NeuAcα2,3Galβ1,4GlcNAc-OR, wherein R is an amino acid, a saccharide, an oligosaccharide or an aglycon group having at least one carbon atom and is linked to or is part of a glycopeptide, and wherein the eukaryotic fucosyltransferase is a recombinantly produced FucT-VI corresponding to SEQ ID NO:1 or FucT-VII fucosyltransferase corresponding to SEQ ID NO:2, and wherein the eukaryotic fucosyltransferase lacks a membrane anchoring domain.

While the '663 patent discloses a FucT-VI, the methods disclosed in the '663 patent are distinct from those of claim 107.

As the Examiner is aware, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP 2131 (quoting *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628 (Fed. Cir. 1987).

Here, the '663 fails to disclose the transfer of fucose to any recombinant polypeptide. That is, upon a review of the '663 patent and in particular the sections cited by the Examiner, Applicants have found no disclosure related to the *in vitro* transfer of fucose to a recombinant polypeptide. The Examiner pointed to column 13 as support for the "use of glycosyltransferase in enzymatic reactions to produce glycoproteins...". However, column 13 is related to the use of recombinant cells to produce glycosylated proteins. For example, column 13, lines 23-30 states:

> For example, recombinant proteins such as tissue plasminogen activator or erythropoietin normally exists as glycoproteins. Should specific oligosaccharide structures on these glycoproteins be shown to have beneficial effects on their biosynthesis, serum half life, receptor interaction, or other function, the reagents and processes provided by the present *invention can be used to construct hosts* that yield recombinant proteins with the specific, and functionally optimal, oligosaccharide structures.

Thus, this section describes recombinant host cells that can be engineered to produce recombinant proteins with the specific and functionally optimal oligosaccharide structure. This is not, however, a description of an *in vitro* reaction as claimed.

Moreover, the Examiner has not pointed to any recitation in the '663 patent that discloses an enzymatic reactions claimed, wherein the glycopeptide has a substantially uniform fucosylation pattern. For at least these reasons, Applicant submit that the '663 patent

fails to disclose each limitation of claim 107. Applicants request the Examiner to withdraw the rejection.

Likewise, the '420 patent fails to disclose at least both of the above-noted claim limitations. That is, we have not identified disclosure in the '420 patent of an *in vitro* method to transfer fucose to a full-length recombinant polypeptide. In addition, the Examiner has not pointed to and we have not identified any disclosure in the '420 teaching an *in vitro* enzymatic reaction wherein fucose is transferred to a full length recombinant polypeptide and resulting in a glycoprotein having a substantially uniform glycosylation pattern.

For at least these reasons, Applicant submit that the '420 patent fails to disclose each limitation of claim 107. Applicants request the Examiner to withdraw the rejection.

Claim 107 is rejected under 35 U.S.C. § 102(e) as allegedly being unpatentable over Lowe (5,324,663 ('193)) or Sasaki (U.S. Patent 7,094,530 ('530)). Applicants respectfully traverse the rejection.

The Examiner states that the '193 patent claims "priority to US Application No.: 09/042,531 filed on 03/17/1998). However, Applicants note that the '193 patent does not claim priority to this application. Rather, the '193 is the patent that issued from the 09/042,531 application. This patent does claim priority to the '663 patent discussed above. In fact, the '193 patent appears to contain the same disclosure as the '663. As such, the response to the rejection based on the '663 patent holds true for the ''193 patent as well. This response is incorporated herein by reference. As above, Applicants respectfully request the Examiner to withdraw the rejection.

Claim 107 also is rejected over Sasaki ('530). Sasaki disclosed a fucosyltransferase and describes the construction of cells expression the fucosyltransferase. In addition, Sasaki disclose an analysis of expression of fucosyltransferase in a variety of cell types. However, Applicants have found no disclosure in Sasaki of an *in vitro* method to transfer fucose to a full-length recombinant glycopeptide. Rather, Sasaki discloses fucosylation of proteins in cells expressing a fucosyltransferase. Sasaki does state that

> Carbohydrate chains can be synthesized *in vitro* using the α-1,3-fucosyltransferase of the present invention. For example, GlcNAc in the lactosamine

structure (Galβ1-4GlcNAc structure) in glycoproteins, glycolipids or oligosaccharides can be provided with fucose in α1→3 linkage. Further, glycoproteins, glycolipids or oligosaccharides which serve as substrates, when treated with the α -1,3-fucosyltransferase of the present invention, can be modified for conversion of the carbohydrate chain structure at the nonreducing end to the sialyl Lewis x structure. (See column 9, lines 30-40.)

However, this does not teach that any of the substrates are full-length recombinant glycopeptides as recited in the claims. The Examiner points to columns 35 and 36 as support for enzyme activity assays. However, Applicants found no mention of the use of recombinant, full-length glycopeptides as substrates. In fact, it appears that only carbohydrate chains were actually described as substrates. Moreover, there is no mention in the '530 patent that any of the resulting fucosylated enzymatic products have substantially uniform fucosylation patterns, as required by the claims. As such, for at least these reasons, the '530 patent fails to anticipate claim 107. Applicants respectfully request that the Examiner withdraw this rejection.

Rejection Under 35 U.S.C. §103

Claims 107 and 108 are rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Lowe ('663)) or Lowe ('420) or Lowe ('193) or Sasaki ('530). Applicants respectfully traverse the rejection.

The law is clear that to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones,* 21 USPQ2d 1941 (Fed. Cir. 1992). Second, there must be a reasonable expectation of success. *In re Merck & Co., Inc.*, 231 USPQ 375 (Fed. Cir. 1986). Third, the prior art reference, or references when combined, must teach or suggest all the claim limitations. *In re Roy*ka, 180 USPQ 580 (CCPA 1974).

In affirming the obviousness analysis that it had set forth in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966), the Supreme Court has also stated that "[t]here is no necessary inconsistency between the idea underlying the TSM [i.e., teaching-suggestion-motivation] test and the *Graham* analysis." *KSR Int'l Co. v. Teleflex Inc.*, No. 04-1350, slip op. at 13 (2007). Thus, the Supreme Court has not invalidated the TSM test, but rather only

rejected its "rigid" application. *See id.* at 11. An obviousness rejection continues to require an explicit analysis providing some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. *See id.* at 14 (citing *In re Kahn*, 411 F.3d 977, 988 (Fed. Cir. 2006)).

The alleged *prima facie* case of obviousness here is deficient because the cited references alone, or in any combination, fail to teach each and every element found in the claims. In particular, the combination of references fails to teach use of a full-length recombinant glycpopeptide as an *in vitro* substrate for fucosyltransferase FucT-VI or FucT-VII.. In addition, the combination fails to teach that the product of the fucosylation reaction results in substrates having substantially uniform fucosylation patterns.

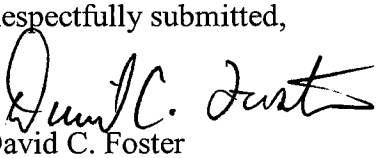
Moreover, Applicants submit that one of skill in the art a the time of filing the Lowe or Sasaki patent applications would not have been motivated to use a recombinantly produced full-length glycopeptide as a substrate for *in vitro* fucosylation reactions as claimed. As can be seen in each of the cited references, in general when fucosylation of proteins was examined it is when the substrate protein and fucosyltransferase were co-expressed in a cell. In contrast, *in vitro* assays consistently used oligosaccharides as substrates. However, not until Applicants invention was it appreciated that "certain FucT molecules are surprisingly more effective at fucosylating glycopeptides." See paragraph 102. Thus, not only is the prior art lacking a teaching of each limitation of the claims, Applicants submit that there was no motivation at the time of the invention to modify the prior art to reach the presently claimed invention. As such, there is no *prima facie* case of obviousness. As such, the Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants respectfully request a telephone interview if the Examiner believes that the claims as amended are not in condition for allowance in light of the response submitted above. The undersigned can be reached at 415-442-1000.

Respectfully submitted,



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